UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO

EXAMINER	
ART UNIT	PAPER NUMBER
	8

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

✓ Responsive to communication(s) filed on July 31, 1996.

✓ This action is **FINAL**.

Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, ichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 36(a).

sposition of Claims

✓ Claim(s) 1-9 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

Claim(s) _____ is/are allowed.

✓ Claim(s) 1-9 is/are rejected.

Claim(s) _____ is/are objected to.

Claims _____ are subject to restriction or election requirement.

plication Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

The drawing(s) filed on _____ is/are objected to by the Examiner.

The proposed drawing correction, filed on _____ is approved disapproved.

The specification is objected to by the Examiner.

The oath or declaration is objected to by the Examiner.

iority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

All Some* None of the CERTIFIED copies of the priority documents have been

received.

received in Application No. (Series Code/Serial Number) _____.

received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

tachment(s)

Notice of Reference Cited, PTO-892

Information Disclosure Statement(s), PTO-1449, Paper No(s) _____

Interview Summary, PTO-413

Notice of Draftsperson's Patent Drawing Review, PTO-948

Notice of Informal Patent Application, PTO-152

Applicant's arguments filed July 31, 1996 have been fully considered but they are not persuasive. The amendment has been entered.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification remains objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an enabling disclosure for reasons of record. Claims 1-9 are drawn to a method of delivering a gene to the central nervous system of a mammal, comprising administering a neurotropic virus containing a DNA sequence of interest where expression of the DNA sequence of interest is regulated by a latency promoter. It is not apparent from the disclosure that the method would sufficiently deliver a gene to the central nervous system such that the host would receive a benefit from such delivery. Applicant has shown that biologically active b-glucuronidase can be expressed when the DNA sequence for the enzyme operatively linked to the LAT promoter is contained in an HSV vector is administered by corneal abrasion. Although b-glucuronidase is detected, there is no evidence that such expression levels would have an effect on the host mammal. There is no evidence that such expression levels for example correlate to a treatment for a b-glucuronidase deficiency. It is not clear

that the delivery of any particular gene or the expression of that gene to any particular level would result in the host having beneficial effect.

Applicant argues that a method of delivering a DNA sequence to the central nervous system is all that is claimed, and that applicant have taught the method to achieve such in the specification. Applicant argues that their is no requirement in the claims that the method of delivery provide a benefit to the host. Applicant argues that the examiner has not provided a reasonable basis for the lack of enablement rejection. Applicant argues that neurotrophic viruses by their name have affinity for the central nervous system, and are well known in the art. These arguments are not persuasive.

The claims are read in light of the specification. In the instant application the specification discloses a method of delivery for purposes of gene therapy (pages 9-10, bridg. parag.). Thus the method of delivery is read as being delivery for gene therapy. As the delivery of the neurotrophic virus containing a DNA sequence of interest has not been shown to achieve any therapeutic benefit to the host, the method of delivery has not been enabled. Thus while applicant has shown the delivery of DNA sequences for b-glucuronidase to the brain via a herpesvirus vector, the claims are not enabled when read in light of the specification. The examiner has read the specification and can not find any disclosure for delivery absent a therapy. As

stated in the previous office action, other neurotrophic viruses and routes of delivery have also not been shown to have a therapeutic effect in a host.

Claims 1-9 remains rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification in the previous office action.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1,2,5 and 6 remain rejected under 35 U.S.C. § 102(b) as being clearly anticipated by Dobson et al (1989) J. Virol. 63, 3844-3851 for reasons of record. Dobson teaches the delivery of the rabbit ß-globin gene to the CNS of mice where expression of the ß-globin gene is regulated by the HSV-1 latency promoter (page 3850, col. 1, parag. 4, lines 1-6, page 3847, figure 5). The HSV-1 vector is administered by foot pad injection which is a peripheral inoculation (page 344, col. 2, parag. 1, lines 4-6). Thus the claims are clearly anticipated by Dobson.

Applicant argues that Dobson teaches the infection of the peripheral nervous system, and not the central nervous system as claimed. This argument is not persuasive. The claims state þcapable of infecting the central nervous systemþ. This does not

preclude the herpesvirus from infecting another cell as a result of the method.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 3,4,7,8 and 9 remain rejected under 35 U.S.C. § 103 as being unpatentable over Dobson et al (1989) J. Virol. 63, 3844-3851 in view of Nishimura et al (1986) Proced. Natl. Acad. Sci. 83, 7292-7296 for reasons of record. Dobson teaches the delivery of the rabbit ß-globin gene to the CNS of mice where expression of the ß-globin gene is regulated by the HSV-1 latency promoter (page 3850, col. 1, parag. 4, lines 1-6, page 3847, figure 5). The HSV-1 vector is administered by foot pad injection which is a peripheral inoculation (page 344, col. 2, parag. 1, lines 4-6). Dobson does not teach the delivery of b-glucuronidase operatively linked to a promoter. However, Nishimura teaches the DNA sequence for b-glucuronidase. Methods for the insertion of

DNA sequence of interest into recombinant HSV-1 vectors as described in Dobson would have been within the scope of skills of the ordinary artisan at the time of the instant invention. Motivation is offered by Dobson in stating that HSV-1 is an vector for the transfer of genes to neurons (page 3850, col. 2, parag. 3, lines 1-2).

Applicant argues that Dobson teaches the infection of the peripheral nervous system and not the central nervous system. Applicant argues that Dobson does not suggest the replacement of the globin DNA sequence with one that is capable of altering neurological function. These arguments are not persuasive.

The claims recite þcapable of infecting the central nervous systemþ, which does not limit the infection to the CNS. Further as the claims are to delivery specifically, there is every reason for an expectation of success in delivery alone given Dobson in view of Nishimura with the cited motivation in the previous office action. Applicant's claims do not require expression or that a neurological alteration be achieved. The claims only require that the DNA sequence be delivered. Dobson shows such and applicant has not provided any reasons as to why mere delivery would not be achieved when the artisan follows Dobson.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for response to this final action is set to expire THREE MONTHS from the date of this action. In the event a first response is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event will the statutory period for response expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Deborah Crouch, Ph.D. whose telephone number is (703) 308-1126.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Dr. D. Crouch
September 11, 1996